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Neurotoxicity of beta-amyloid and prion peptides.

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Abstract

Neuropathological observations, supported by genetic and biochemical studies, indicate the central role of amyloid-beta protein deposits in the pathogenesis of Alzheimer's disease. In prion-related encephalopathies also, an altered form of prion protein forms amyloid fibrils and accumulates in the brain. In both conditions the amyloid deposition is accompanied by nerve cell loss, the pathogenesis and molecular basis of which are not understood. Synthetic peptides homologous to amyloid-beta protein and its fragments and to prion protein fragments are utilized to investigate the mechanisms of cerebral deposit formation and the role played by these proteins in Alzheimer's disease and prion-related encephalopathies, respectively. Amyloid-beta protein peptides have been shown to be neurotoxic and amyloidogenic under experimental conditions and numerous studies have been performed to clarify the mechanism of neuronal death induced by exposure to these peptides. Peptides homologous to the fragment 106-126 of prion protein, an integral part of all abnormal prion protein isoforms that accumulate in the brain of patients with prion-related encephalopathies, are neurotoxic, fibrillogenic, and have a secondary structure largely composed of beta-sheet and proteinase-resistant properties.

MeSH

Alzheimer Disease; Amyloid beta-Protein; Brain; Human; Nerve Degeneration; Neurofibrillary Tangles; Peptide Fragments; Prion Diseases; Prions; Support, Non-U.S. Gov't

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can be used to provide a complete diagnosis for all potential CF carriers or patients. A complete description of these procedures is later described.

The invention therefore provides a method and kit
5 for determining if a subject is a CF carrier or CF patient. In summary, the screening method comprises the steps of:

providing a biological sample of the subject to be screened; and providing an assay for detecting in the
10 biological sample, the presence of at least a member from the group consisting of a 507 mutant CF gene, 507 mutant CF gene products and mixtures thereof.

The method may be further characterized by including at least one more nucleotide probe which is a different
15 DNA sequence fragment of, for example, the DNA of Figure 1, or a different DNA sequence fragment of human chromosome 7 and located to either side of the DNA sequence of Figure 1. In this respect, the DNA fragments of the intron portions of Figure 2 are useful in further
20 confirming the presence of the mutation. Unique aspects of the introns at the exon boundaries may be relied upon in screening procedures to further confirm the presence of the mutation at the I507 position or othe mutant positions.

25 A kit, according to an embodiment of the invention, suitable for use in the screening technique and for assaying for the presence of the mutant CF gene by an immunoassay comprises:

(a) an antibody which specifically binds to a gene
30 product of the mutant CF gene having a mutation at one of the positions of 85, 148, 178, 455, 493, 507, 542, 549, 551, 560, 563, 574, 1077 and 1092;

(b) reagent means for detecting the binding of the antibody to the gene product; and

35 (c) the antibody and reagent means each being present in amounts effective to perform the immunoassay.

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